OBLON
SPIVAK
MCCLELLAND
MAIER
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P.C.

ATTORNEYS AT LAW
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CONTROLLER
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KMORSBERGER@OBLON.COM

January 18, 2005

UNITED STATES PATENT AND TRADEMARK OFFICE
Box 16
Washington, DC 20231

Attn: Frank Lebron
Refund Department

Re: Deposit Account #150030

Dear Mr. Lebron:

Enclosed is a copy of a portion of our Deposit Account Statement of December, 2004. Please review the highlighted charge on **Serial Number 10/500,891 in the amount of $86.00 on fee code #1614.**

An American Express charge for $1,422.00 was included with the filing of this application. This payment included $430.00 for 5 additional independent claims. **A preliminary amendment was filed with the reissue application, which eliminated the multiple dependencies but still only contained 8 independent claims (see attached claim chart). Please note that although claims 16 and 24 appear to be independent claims, there is a reference to another claim toward the end of the claim language. Therefore, no additional fees are due.**

Please investigate this charge and **kindly refund $86.00 to Deposit Account #150030.** Copies of the appropriate paperwork are attached. If you have questions, please do not hesitate to contact me. My phone number is 703-412-6296.

Sincerely,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Adjustment date: 05/18/2005 RWHITE1
12/03/2004 AJOHNSO2 00000004 150030 10500891
01 FC:1614 86.00 CR

Debra J. Noel
Accounting Department

Enclosures

United States Patent and Trademark Office

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Deposit Account Statement

Requested Statement Month:	December 2004
Deposit Account Number:	150030
Name:	NORMAN F. OBLON
Attention:	
Address:	1940 DUKE STREET
City:	ALEXANDRIA
State:	VA
Zip:	22314

DATE	SEQ	POSTING REF TXT	ATTORNEY DOCKET NBR	FEE CODE	AMT	BAL
12/01	3	10256081	228407US0	1202	$54.00	$34,159.71
12/01	5	09591789	260895US96	8021	$40.00	$34,119.71
12/01	11	09512735	0059-1196-2D	1460	-$130.00	$34,249.71
12/01	32	10937852	257598US0COUNT	1202	$36.00	$34,213.71
12/02	1	10901264	251752US0CONT	1806	$180.00	$34,033.71
12/02	6	10330120	232209US0SHB	1806	$180.00	$33,853.71
12/02	11	10660635	242829US90	1254	$1,530.00	$32,323.71
12/02	202	0147750983	241119TW/TEP/FF	8014	$25.00	$32,298.71
12/02	240	10728860	241119TW/TEP/FF	8007	$20.00	$32,278.71
12/03	5	10500891	255062US0PCT	1614	$86.00	$32,192.71
12/03	32	11001319	262548US6	1202	$18.00	$32,174.71
12/03	33	11001319	262548US6	1203	$300.00	$31,874.71
12/03	191	10831363	252483US0CONT	1001	$150.00	$31,724.71
12/06	1	10031339	217926US0PCT	1460	$130.00	$31,594.71
12/06	2	10269044	~~10269044~~ 229392US	1806	$180.00	$31,414.71
12/06	3	10204426	227573US	9204	-$280.00	$31,694.71
12/06	4	09720523	~~PM275480~~ 236088US	1202	$108.00	$31,586.71
12/06	56	10717663	245871US/KQU	1202	$18.00	$31,568.71
12/06	153	08719891	~~N0003/7006~~ 253529US	1462	$270.00	$31,298.71
12/07	1	09949120	213751US0SRD	1202	$162.00	$31,136.71
12/07	3	09969758	214757US0	1202	$90.00	$31,046.71
12/07	9	10498214	254412US0PCT	1615	$324.00	$30,722.71
12/07	88	0145610688	235852CA/TEP/FF	8014	$25.00	$30,697.71
12/07	165	60531677	247140US/KQU	8007	$80.00	$30,617.71
12/07	167	10740428	247077US/KQU	8007	$100.00	$30,517.71
12/08	3	09647907	10939/1000	1202	$18.00	$30,499.71
12/08	4	10244008	21581-280-US	1806	$180.00	$30,319.71
12/08	8	60606884	258374US0PROV	1807	$50.00	$30,269.71

Due Date July 9, 2004

OSMM&N File No. 255062US0PCT By NFO/dty/FF

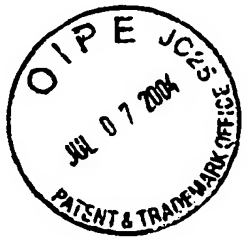
Serial No. New U.S. PCT Application based on PCT/FR03/00129

In the matter of the Application of Joel COTTON, et al.

For PHOSPHINIC PSEUDOPEPTIDE DERIVATIVES FOR THE SELECTIVE INHIBITION OF THE C-TERMINAL ACTIVE SITE OF ANGIOTENSIN I CONVERTING ENZYME (ACE)

The following has been received in the U.S. Patent Office on the date stamped hereon:

- 61 pgs. Specification 17 Claims (English Translation) pgs. Sequence Listing
- Combined Declaration, Petition & Power of Attorney (3 pages)
- Application Data Sheet
- Notice of Priority
- Dep. Acct. Order Form
- Credit Card Payment Form for $1,422.00
- Drawings (3 sheets)
- PCT Transmittal Letter
- Preliminary Amendment
- PCT/IB/304
- PCT/IB/308
- International Search Report
- Request for Consideration of Documents Cited in International Search Report



SERIAL NO. _____

DATE RECEIVED _____

FORM PTO-1390 (Modified) (REV. 11-2000) U.S. DEPARTMENT OF .MERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATT EY'S DOCKET NUMBER: **255062US0PCT**

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR03/00129	**16 JANUARY 2003**	**18 JANUARY 2002**

TITLE OF INVENTION

PHOSPHINIC PSEUDOPEPTIDE DERIVATIVES FOR THE SELECTIVE INHIBITION OF THE C-TERMINAL ACTIVE SITE OF ANGIOTENSIN I CONVERTING ENZYME (ACE)

APPLICANT(S) FOR DO/EO/US

Joel COTTON, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☒ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☐ Express Mail Label No.
23. ☒ Other items or information:

Application Data Sheet
Notice of Priority
PCT/IB/304
PCT/IB/308
Request for Consideration of Documents Cited in International Search Report
Drawings (3 Sheets)

U.S. APPLICATION NO. (IF KNOWN, SEE : R	INTERNATIONAL APPLICATION NO. PCT/FR03/00129	ATTORNEY'S DOCKET NUMBER 255062US0PCT

24. The following fees are submitted:.	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1080.00		
☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $920.00		
☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $770.00		
☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $730.00		
☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$920.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	$0.00	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	24 - 20 =	4	x $18.00	$72.00	
Independent claims	8 - 3 =	5	x $86.00	$430.00	
Multiple Dependent Claims (check if applicable).			☐	$0.00	
TOTAL OF ABOVE CALCULATIONS =				$1,422.00	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				$0.00	
SUBTOTAL =				$1,422.00	
Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)). +				$0.00	
TOTAL NATIONAL FEE =				$1,422.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). ☐				$0.00	
TOTAL FEES ENCLOSED =				$1,422.00	
				Amount to be: refunded	$
				charged	$

a. ☐ A check in the amount of _____ to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees.

c. ☒ The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 15-0030

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Telephone No.: 703-413-3000
Fax No.: 703-413-2220
Customer Number: 22850

SIGNATURE

Norman F. Oblon

NAME

24,618

REGISTRATION NUMBER

DATE

PTO-2038 (02-2003)
Approved for use through 02/28/2006. OMB 0651-0043
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United States Patent & Trademark Office

Credit Card Payment Form
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Credit Card Information	
Credit Card Type: ☒ **American Express**	
Credit Card Account #: [redacted]	
Credit Card Expiration Date: December 31, 2005	
Name as it Appears on Credit Card: Tyson, Derrick L	
Payment Amount: $(US Dollars): 1,422.00	
Signature:	Date: July 6, 2004
The Commissioner is hereby authorized to charge any additional fees which may be required for the papers being filed herewith and for which no credit card payment can be processed, or credit any overpayment to Deposit Account No. 15-0030.	

Credit Card Billing Address	
Street Address 1: Oblon, Spivak, McClelland, Maier & Neustadt, P.C.	
Street Address 2: 1940 Duke Street	
City: Alexandria	
State: Virginia	Zip/Postal Code: 22314
Country: U.S.A.	
Daytime Phone #: (703) 413-3000 Accounting Dept.	Fax #: (703) 413-2220

Request and Payment Information
Description of Request and Payment Information: NEW U.S. PCT APPLN.
Application No.:
Patent/Registration No.:
Docket No.: 255062US

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Form #: 14051

__ PGS. OF SPECIFICATION
3 SHEET(S) OF DRAWINGS
1 PRIORITY(IES) CLAIMED
NO SMALL ENTITY

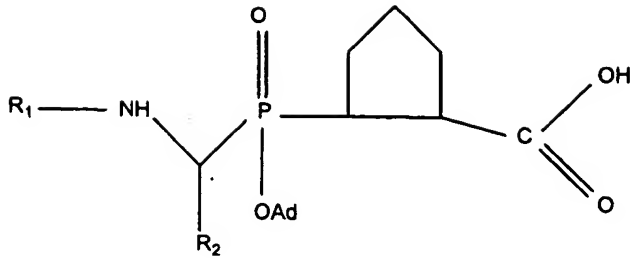
CLAIM CALCULATION SHEET

INTERNATIONAL PCT NO:

DOCKET NO:

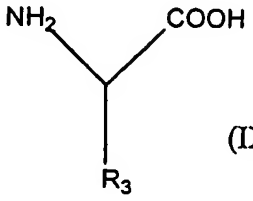
CLAIM	INTERNATIONAL PCT APPLICATION AS FILED		AFTER AMENDMENT IN INTERNATIONAL PHASE		AFTER PRELIMINARY AMENDMENT		AFTER 1ST AMENDMENT	
	IND.	DEP.	IND.	DEP.	IND.	DEP.	IND.	DEP.
1	1				1			
2	1				1			
3		1				1		
4		3				1		
5		(1)				1		
6		(1)				1		
7		(1)				1		
8		(1)				1		
9	1				1			
10	1				1			
11	1				1			
12		3				1		
13	1				1			
14	1				1			
15		1				1		
(16)		2				1		
17	1				1			
18						1		
19						1		
20						1		
21						1		
22						1		
23						1		
(24)						1		
25								
26								

TOTAL IND.			8	
TOTAL DEP.			16	
TOTAL			24	



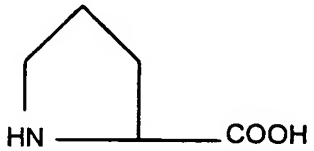
(VIII)

5) coupling the compound of formula (VIII) with the amino acid of formula (IX) or (X):



(IX)

or



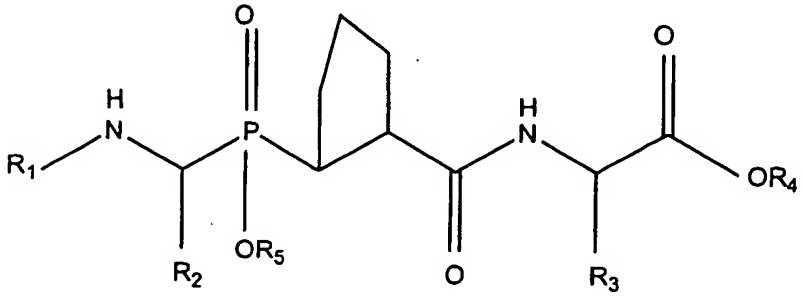
(X)

in which R_3 is as defined above, and

6) removing the protecting group Ad.

Claim 15 (Currently Amended): ~~Process according to~~ A process as claimed in Claim 14, ~~in which~~ wherein the peptide coupling step 5) is performed via solid-phase peptide synthesis ~~using as~~ wherein the solid phase is a resin substituted with the amino acid of formula (IX) or (X).

Claim 16 (Currently Amended): A process ~~Process~~ for preparing a pseudopeptide of formula:

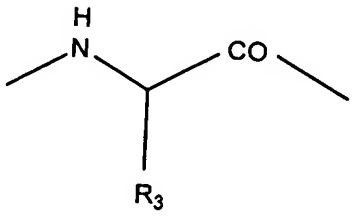


(II)

~~in which:~~ wherein,

- R_1 represents a protecting group for an amine function, or an amino acid or a peptide protected with a protecting group for an amine function,

- R_2 and R_3, which may be identical or different, represent the side chain of a natural or unnatural amino acid, the sequence:



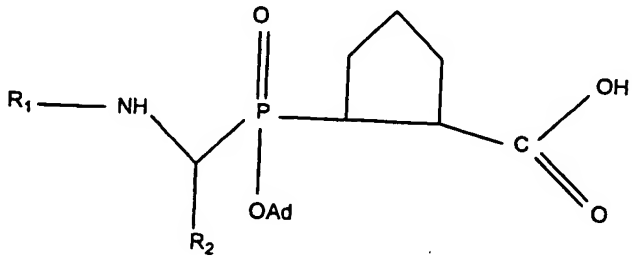
also possibly forming the Pro residue,

- R_4 represents a hydrogen atom, and

- R_5 represents a group ~~capable of forming~~ that can form an *in vivo* hydrolysable phosphinic ester;

~~in which~~ wherein the phosphinic function of the pseudopeptide obtained via the process of Claim 14 ~~or 15~~ is esterified by coupling with an alcohol of formula R_5OH or by reaction with a halide of formula R_5X in which X represents a halogen atom.

Claim 17 (Currently Amended): A compound ~~Compound~~ of formula (VIII):



(VIII)

wherein ~~in which~~:

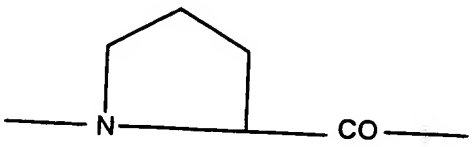
- R_1 represents a protecting group for an amine function or an amino acid or a peptide protected with an amine function, and

- R_2 represents the side chain of a natural or unnatural amino acid.

Claim 18 (New): The method of Claim 2, wherein R_2 represents the benzyl, methyl or phenylethyl group.

Claim 19 (New): The method of Claim 2, wherein R_3 represents the side chain of alanine, arginine or tryptophan.

Claim 20 (New): The method of Claim 2, wherein the sequence –NH-CH(R_3)-CO- forms the Pro residue:

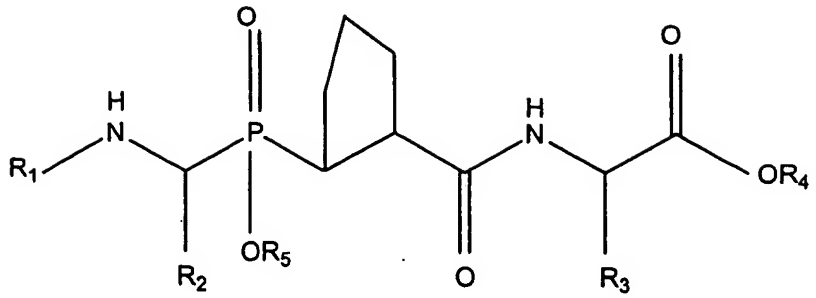


Claim 21 (New): The method of Claim 2, wherein R_4 and/or R_5 represent(s) a hydrogen atom.

Claim 22 (New): A pharmaceutical composition comprising at least one phosphinic pseudopeptide derivative as claimed in Claim 10.

Claim 23 (New): A pharmaceutical composition comprising at least one phosphinic pseudopeptide derivative as claimed in Claim 11.

Claim 24 (New): A process ~~Process~~ for preparing a pseudopeptide of formula:

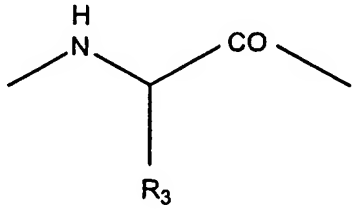


(II)

wherein,

- R_1 represents a protecting group for an amine function, or an amino acid or a peptide protected with a protecting group for an amine function,

- R_2 and R_3, which may be identical or different, represent the side chain of a natural or unnatural amino acid, the sequence:



also possibly forming the Pro residue,

- R_4 represents a hydrogen atom, and

- R_5 represents a group that can form an *in vivo* hydrolysable phosphinic ester;

wherein the phosphinic function of the pseudopeptide obtained via the process of Claim 15 is esterified by coupling with an alcohol of formula R_5OH or by reaction with a halide of formula R_5X in which X represents a halogen atom.

UNITED STATES PATENT & TRADEMARK OFFICE
Washington, D.C. 20231

1/18/05

REQUEST FOR PATENT FEE REFUND

1 Date of Request: 1/18/05 | 2 Serial/Patent # 10/500891

	3 Please refund the following fee(s):	4 PAPER NUMBER	5 DATE FILED	6 AMOUNT
X	Filing			$
	Amendment			$
	Extension of Time			$
	Notice of Appeal/Appeal			$
	Petition			$
	Issue			$
	Cert of Correction/Terminal Disc.			$
	Maintenance			$
	Assignment			$
X	Other Claim fees			$ 86

7 TOTAL AMOUNT OF REFUND: $ 86

8 TO BE REFUNDED BY:

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- [X] Credit Deposit A/C #: 9 15--0030

10 REASON:

- [X] Overpayment
- [ ] Duplicate Payment
- [ ] No Fee Due (Explanation):

11 REFUND REQUESTED BY:

TYPED/PRINTED NAME: Rita White TITLE: Legal Instrument Examiner

SIGNATURE: Rita White PHONE: 571 308-9140 ext 231

OFFICE: DO/EO

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Refund Branch
Crystal Park One, Room 802B

FORM PTO 1577
(01/99)